# A COMPARATIVE STUDY OF EPIDURAL NALBUPHINE WITH BUPIVACAINE VS BUPIVACAINE ALONE IN INFRA UMBILICAL SURGERIES

## A STUDY OF 100 CASES

**DISSERTATION SUBMITTED FOR THE DEGREE OF**

## DOCTOR OF MEDICINE
**BRANCH – X (ANAESTHESIOLOGY)**

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**CHENNAI, TAMILNADU**

# BONAFIDE CERTIFICATE

This is to certify that this dissertation entitled **"A COMPARATIVE STUDY OF EPIDURAL NALBUPHINE WITH BUPIVACAINE VS BUPIVACAINE ALONE IN INFRA UMBILICAL SURGERIES"** is bonafide record work done by **Dr. R. CHITHRA DEVI** under my direct supervision and guidance, submitted to the Tamil Nadu Dr. M.G.R. Medical University in partial fulfillment of University regulation for MD, Branch X – Anaesthesiology.

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# DECLARATION

I **Dr. R. CHITHRA DEVI** solemnly declare that this dissertation titled **"A COMPARATIVE STUDY OF EPIDURAL NALBUPHINE WITH BUPIVACAINE VS BUPIVACAINE ALONE IN INFRA UMBILICAL SURGERIES"** has been done by me. I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree, diploma to any other University board either in India or abroad.

This is submitted to The Tamilnadu Dr. M. G. R. Medical University, Chennai in partial fulfillment of the rules and regulation for the award of Doctor of Medicine degree Branch –X (Anaesthesiology) to be held in March 2010.

**Place :** Madurai **Dr. R. CHITHRA DEVI**.

**Date :**

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# INTRODUCTION

The relief of pain during surgery is the raison d'etre of anaesthesia. The international association for the study of pain has defined "pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage". Pain is always under estimated and under treated.

Analgesia, one of the components of triad of anaesthesia, has now extended to relief of post operative pain, chronic pain and cancer pain. It is achieved by use of drugs administered through different routes and techniques among which the spinal route of analgesia plays an important role in the intra and post operative period. Effective postoperative analgesia reduces post operative morbidity allows early ambulation and discharge.

The spinal cord has taken the center stage in analgesia practice following the demonstration of analgesia with intrathecal morphine by Yaksh and Rudy (1977). Deposition of drugs in the epidural and subarachnoid space paved a new era for pain relief.

# HISTORY

- Melzack and walls (1965) propounded the gate control theory of pain.
- Reynolds (1969) described the endogenous neuronal system of analgesia.
- Pert and Synder (1973) discovered the opioid specific receptors in the substantia gelatinosa of spinal cord and brain.
- Martin and coworkers have classified the opioid receptors into three types.
- Wang et al (1979) first applied intrathecal opioids for relief of pain.
- Michael J. Cousins et al (1979) demonstrated the use of epidural morphine for analgesia.
- Glynn et al 1981 studied the pharmacokinetics and analgesic response of epidural meperidine in man.

# AIM OF THE STUDY

To compare the effects of epidural Nalbuphine and 0.5% Bupivacaine with that of 0.5% Bupivacaine alone in infra umbilical surgeries with respect to:

- Onset of sensory blockade
- Onset of motor blockade
- Post operative analgesia
- The quality of analgesia

# ANATOMICAL CONSIDERATIONS

The epidural space is a potential space within the bony cavity of the spinal canal and outside dural sac. It extends from the foramen magnum to the coccyx. Within the cranium the endosteal and meningeal layers are united but below the foramen magnum the two layers are separate, the outer becoming the periosteal lining of the spinal canal duramater. Between these 2 layers lies the epidural space. The spinal canal is triangular in cross-section and the epidural space is widest in midline posteriorly in the lumbar region averaging about 5-6mm in diameter. In the mid thoracic region the distance is somewhat less in the range of 3-5mm in the midline.

BOUNDARIES OF EPIDURAL SPACE

Above : the foramen magnum where the periosteal and spinal layers of the dura fuse together.

Below : the sacrococcygeal membrane

Front : the posterior longitudinal ligament covering the posterior aspect of vertebral bodies and intervertebral disc.

Behind : the anterior surface of vertebral lamina and ligametum flavum

Laterally : the pedicles of vertebra and intervertebral foramina with the paravertebral spaces. Fibrous strands anchoring the dura posteriorly, party divides the epidural space in the midline so that injected fluid frequently divides the space laterally rather than in the midline.

Ligamentum flavum is concerned with the identification of the epidural space. It is composed of yellow elastic fibres. It is thinnest in the cervical region becoming thicker lower down. The spine is thickest in the lumbar region.

**SIZE OF THE EPIDURAL SPACE**

| REGION | EPIDURAL SPACE | THICKNESS OF DURA |
|---|---|---|
| Cervical | 1 - 1.5 mm | 1.5 - 2mm |
| Upper thoracic | 2.5 - 3 mm | 1 mm |
| Lower thoracic | 4 - 5 mm | 1 mm |
| Lumbar | 5 - 6 mm | 0.66 - 0.33 mm |

CONTENTS OF THE EPIDURAL SPACE

It includes dural sac and spinal nerve roots, extra dural plexus of veins (Batson's) lymphatics and fat. The 31 pairs of spinal nerves with their dural cuff traverse the space on their way to intervertebral foramina. The veins receive tributaries from the

adjacent bony structures and the spinal cord. They communicate with the venous rings at each vertebral level with the basivertebral veins in the posterior aspect of each vertebral body and with the ascending, deep cervical, intercostals, ileo lumbar and lateral sacral veins. The veins have no valves and constitute the valveless vertebral venous plexus of Batson.

They connect the pelvic veins below with the intracranial veins above, so that air or local analgesic solution injected may ascend to the brain. They drain into interior vena cava via the azygos vein.

The epidural veins become distended during coughing and straining and when inferior vena cava is obstructed or in late pregnancy. The intrathoracic pressure is conducted via the paravertebral space to the thoracic epidural space and to a diminishing extent to the cervical and lumbar region.

ANATOMY OF THE LUMBAR VERTEBRA

The bodies of the lumbar vertebra are large and kidney shaped, the vertebral foramen in roughly triangular. The pedicles are thick with shallow superior notches. The transverse processes are slender the laminae are short, broad and strong and do not

overlap each other. The spinous processes are horizontal and oblique.

**LOCATION OF SPINAL SEGMENTS IN RELATION TO THE VERTEBRAE**

| SPINAL CORD | SEGMENT | VERTEBRAL LEVEL |
|---|---|---|
| Cervical | 1-8 | cervical 1-7 |
| Thoracic | 1-4 | thoracic1-3 |
| thoracic | 5-12 | thoracic4-10 |
| Lumbar | 1-5 | thoracic T10-12 |
| Sacral | 1-5& coccygeal | lower half ofT12-L1 |

# IDENTIFICATION OF EPIDURAL SPACE

In 1921 fidel pages identified the lumbar epidural space with the " sense of give" that is felt by the operator when the needle escapes from the tough ligamentum flavum and enters the epidural space.

The current methods of identifying the lumbar epidural space fall into 2 groups. Those dependent on

1) loss of resistance to injection
2) The negative pressure in the epidural space.

**I Loss of resistance of injection – the test of Sicard, Forestier and Dogliotti:**

This technique is based on the fact that there is a considerable loss of resistance to injection through the needle as it advances the tough ligamentum flavum into epidural space. Either a liquid filled or air filled system can be used to identify this loss of resistance.

Various mechanical aids can be used to facilitate the appreciation of loss of resistance namely.

i) Macintosh's needle with spring loaded stylet.

ii) Brunner and like's spring loaded syringe.

iii) Macintosh's balloon indicator.

iv) Zelenka's 'U' tube and balloon indicator.

**II. Negative pressure sign:**

A negative pressure is present in 80% of the lumbar epidural spaces. The reasons for it are

i) An artifact created by indentation of the dura with the advancing needle

ii) Flexion of the spine

iii) Transmission of the negative intrapleural pressure via the paravertebral spaces to the epidural space.

Negative pressure in the epidural space is not the same at all levels. In the sacral canal it is absent and it is lower in the thoracic region than in the lumbar part of the space.

This negative pressure can be appreciated by:

**Hanging Drop sign of Gutierrez.**

The epidural needle is placed in the interspinous ligament and a drop of fluid is placed in the hub of the needle. As the needle is advanced into the epidural space, due to the negative pressure, fluid is sucked in.

Various mechanical aids can be used to identify this negative pressure namely.

i) 'U' tube manometer

ii) Aneroid manometer

iii) Zorrauin's Bulb indicator

iv) Odom's indicator

v) Brook's indicator

vi) Zelenka's balloon indicator

vii) Dawkin's gravity indicator

**Mechanism of action of drugs injected into epidural space:**

The precise mode of action of an epidural analgesia remains to be totally explained. Theories of mechanism of action, centre around one or more of the following sites.

i) Mixed spinal nerves in the paravertebral space.

ii) Dorsal root ganglia.

iii) Spinal roots within the dural root sleeves.

iv) Subpial region.

**Possible sites of action:**

i) Paravertebral block – probably non-essential.

ii) Intradural spinal roots – probably the principal and essential site of action.

iii) Spinal cord – blocked subsequent to blockade of nerve roots.

## DISTRIBUTION OF THE DRUG GIVEN INTO THE EPIDURAL SPACE

Following epidural injection, the longitudinal spread depends on the remaining volume of solution, since some volume is expected to leak out of the epidural space. Some of this penetrate

the epineurium and perineurium into the sub perineural space. This then spreads subpially to reach the neuraxis. Hence vascular mechanisms are involved in the neural uptake. High concentrations of local anaesthetics in the intradural roots suggests dural root sleeves with arachnoid granulations are likely to be the principal site of penetration through the dural barrier.

From the dural sleeves, the drug spreads in the subdural space with further penetration into subarachnoid and subpial space from where the local anaesthetics enter into the nerve roots and the spinal crod.

**FACTORS AFFECTING THE SPREAD OF THE LOCAL ANAESTHETIC:**

**1. Age**

Dose requirements rise steeply during the period of growth and maturation and when the body growth has reached its limits the opposing effects of senescence become unmasked and there is a progressive reduction in the dose requirements as age advances.

The increase in dose during maturation is due to

(i) Expanding spinal cylinder

(ii) Increased binding site

The decrease in dose requirement during old age is due to

i) Impaired tissue barriers

ii) Reduction in the number of binding sites

iii) Declining neuronal population

**ii. Height of the individual**

Volume of the epidural space is proportional to its length which is related to body height. As per a study by Bromage in 1962, there is a tendency towards increasing dose requirements with increasing height. But the statistical association is weak. Thus while the length of the spinal cylinder can be taken into account when the dosage requirements are being computed, for all practical purposes, it can be ignored except in extremely short and extremely tall. For bupivacaine 0.5%, it has been advocated to use 1ml/segment to be blocked for 150cm (5ft.) of height plus. 1ml/segment for each 5cm over 150cm.

**iii. Atherosclerosis:-**

In atherosclerotic individuals, the dosage requirements are reduced much below the predicted chronological level. The same dosage level results in a 40-50% increase in the segmental spread. The latency of onset is delayed by 35%.

This is due to

i) Prematurely declining neuronal population.

ii) Changes in the ground substance.

**iv. Increased intra abdominal pressure:**

The dosage requirements have to be reduced by about 33%. This is due to diversion of a proportion of venous return through the internal vertebral venous plexus which become engorged and thus reducing the volume of the epidural space thereby increasing the spread.

**v. Site of injection:-**

The drug preferentially acts in the segments close to the site of injection. Hence it is suggested to give the drug in the mid space of the desired blockade.

**vi. Speed of injection:**

With rates between 0.3ml/sec to .75ml/sec, the spread is the same. Abnormally faster and slower rates are likely to alter the spread of epidural solution.

**vii. Posture:**

There is slight but significant difference between dosage requirements in patients sitting and supine. Since gravity favours downward spread, it is worthwhile to exploit gravity to favour spread. However the magnitude of influence is not great.

**viii. Volume concentration and composition of local anaesthetic solution:**

Increasing dosage produces a linear increase in the duration of sensory block.

Increasing the concentration reduces the onset time and increases the intensity of block.

Increasing the volume injected increases the longitudinal spread of solution and also the duration of block.

# PHYSIOLOGICAL CONSIDERATIONS

There are two components of pain, neurophysiologically mediated sensory component and an emotional component.

**There are two types of pain**

1. Physiological pain is a transient sensation due to noxious, mechanical, thermal, chemical stimulus each with a clearly defined threshold and without causing damage to the nervous system.
2. Pathological pain is an inflammatory response to tissue injury or damage to central nervous system with an alteration in perception. Pain following surgery is pathological

There are two major theories of pain:

1. SPECFICITY THEORY proposed by Von Frey states the pain is due to stimulation of specific end organs.
2. INTENSIVE SUMMATION pattern theory proposed by Gold Scheider states that there are no specific pain receptors and any sensory stimulus if sufficiently severe would produce pain.

## ORGANISATION OF PAIN PATHWAYS

According to the recent theory pain pathway is organized as follows.

Receptors: Nociceptive receptors are fine, profusely branched, free nerve endings covered by Schwann cells with little or no myelin.

There are three types of receptors:

1. Mechano-sensitive nociceptors activated by mechanical stimuli
2. Mechano thermal nociceptors activated by mechanical and thermal stimuli more than 43 degree Celsius
3. Polymodal pain receptors respond to mechanical, thermal and chemical stimuli like hydrogen and potassium ions, histamine, serotonin, bradykinin, prostaglandins, substance P.

FIRST ORDER NEURONS

Mechanosensitive and mechano- thermal pain receptors transmit impulses through thinly myelinated Adelta fibres of 1-5 micrometer diameter with conduction velocity of 15-30mts per second. This is responsible for fast pain which is sharply localize. Polymodal pain receptors transmit impulses through unmyelinated C fibres of 0.4-1.1 micrometer diameter with conduction velocity of 0.5-2 meter per second. This is responsible for the poorly

localized slow pain. Transmission through both these fibres causes the “Double response of Lewis”. The peripheral afferent fibres have their cell body in the dorsal root ganglion and project via the lateral part of the dorsal root called “Tract of Lissauer. They terminate in dorsal horn of spinal cord with 1-2 segments of entry. A delta fibres terminate in lamina 1 (marginal cell layers of Waldeyer) and lamina 5 (wide dynamic range of neurons which respond to their modalities also). Un myelinated c fibres terminate in lamina 2&3 (substantia gelatinosa)

**SECOND ORDER NEURONS**

They arise from the cells and connect with ventral and lateral horn cells in the same and adjacent spinal segments and sub serve both somatic and autonomic reflexes. About 75% of other sensory neurons project contra laterally after decussating in the anterior commissure 1-3 segments higher than the root of entry and divide into 2 descending tracts.

**NEO SPINOTHALAMIC-LATERAL SPINOTHALMIC TRACT**

It ascends in the antero lateral funiculus of spinal cord to brain stem and thalamus and contains fast conducting fibers which transmit specific localized pain. The fibres are arranged in such a

way that fibres from lower part of body are superficial and from upper art of the body are inner most.

**PALEOSPINOTHALAMIC-VENTRALSPINOTHALAMIC-TRACT:**

It is medially placed and contains slowly conducing fibres responsible for ”second pain” and has connections with reticular core of brain stem limbic and subcortical regions.

**AUXILLARY PAIN CONDUCTING PATHWAYS:**

Thalamic in the nucleus ventro postero lateralis which is the major sensory relay nucleus. The other fibres terminate in the posterior group of nuclei which includes nucleus ventralis posteromedialis, intralaminar nuclei, ventrobasal complex and hypothalamic nuclei.

**THIRD ORDER NEURONS**

Posterior thalamic nuclei project to the post central cortex and upper bank of sylvian fissure and sub serve tactile and proprioceptive stimuli with discriminative sensory function.

**Perception of pain :**

The threshold of perception of pain is the lowest intensity of stimulus recognized as pain. The conscious awareness or perception of pain occurs when the thalamo cortical pathway is destroyed. Somato sensory cortex is essential for the accurate localization, appreciation of intensity and other discriminative aspects of pain. Prefrontal cortex subserves the unpleasant affective and emotional reaction to pain.

**GATE CONTROL THEORY OF PAIN :**

It was propounded by Melzack and Walls in 1965. It states that modulation of pain transmission via the spinothalamic tract through the stimulation of large afferent fibres excite the inhibitory cells in laminar 2 & 3 of dorsal horn which in turn cause pre and post synaptic inhibition of secondary transmission neurons (T cells) in lamina 5 of dorsal horn and interrupt pain pathway. Conversely stimulation of small pain afferents (c fibres) inhibit the T cells in the excitatory state thus facilitating transmission of pain.

## CENTRAL SENSITISATION OR WIND UP

Prolong nociceptive stimulations leads to hyperexcitability of dorsal horn cells and increased cephalad transmission resulting in increased pain sensation. This is responsible for chronic pain syndromes. Descending inhibiting pathways and endogenous pain control mechanisms. It extends from the hypothalamus along the periventriculars and periaqueductal grey matter which communicate through dorso lateral funiculus to end in the nucleus raphe magnus and locus caeruleus. Stimulation anywhere along this tract releases endogenous opioid like peptides and endorphins which activate serotoninergic pathway via descending reticulobulbar spinal system and interact with lamina 1 and 2 of the dorsal horn and exert analgesia. Another descending inhibitory pathway arises from locus caeruleus in pons and projects directly to the spinal cord. Here neurotransmitter is nonadrenaline and this pathway inhibits pain responses in spinal cord by alpha 2 adrenergic mechanism.

**ENDOGENOUS OPIOIDS AND OTHER NEURO TRANSMITTER AND SPINAL MODULATION OF PAIN PERCEPTION.**

There are 5 endorphins. Metenkephalin, leuenkephalins, betaendorphin, alpha endorphin and R endorphin.

**METENKEPHALIN AND LEUENCEPHALIN:**

They are inhibitory neurotransmitters at the site where primary processing of afferent nociceptive information occurs in laminar 1,2,5 of dorsal horn. They act through release of substance P.Dynorphins: Control nociception at the spinal cord level through activation of kappa receptors. It is present in lamina1-5 of dorsal horn.

**BETA-ENDORPHINS**

It is a fragment of the pituitary hormone of beta-lipotropin. It activates descending serotoninergic pathways and suppresses the nociceptive response of spinothalamic neurons. It acts on epsilon receptors and modulates nociceptors during stress.

L-endorphins and R – endorphins are breakdown products of beta endorphins.

SUBSTANCE P (substance preparation) it is a II amino acid peptide. It acts on excitatory transmitter in laminar 1,2,4 and 5 of dorsal horn, spinal trigeminal nucleus and type B cells in dorsal root ganglia. It is released in vivo by the activity of Adelta and C fibres. Endogenous opiates inhibit presynaptic pathway inhibit the action of substance P at the post synaptic level thus inhibiting pain transmission.

**SOMATOSTATIN :**

It is a 13 aminoacid peptid found in lamina 2 of dorsal horn and inhibits function of afferent pain fibres.

## PHARMACOLOGICAL CONSIDERATIONS

**Opioid receptors**: Stereospecfic binding sites called receptors for opioid drugs are present in the cortex, limbic system, hypothalamus, medial thalamus, periaqeductal grey matter, substantia gelatinons. High density of opioid receptors are present in the substantia gelatinosa at the presynaptic and post synaptic site of C delta and C fibre input. Martin and coworkers have classified opiod receptors in to 5 major groups Mu (Mu1, Mu2) kappa (k1,k2,k3) sigma, delta, epsilon. Mu 1 receptor causes supra spinal analgesia and delta causes spinal analgesia on stimulation kappa receptors of which k1 causes spinal analgesia and k3 supra spinal analgesia.

## NALBUPHINE

**Chemistry:**

Nalbuphine hydrochloride is an agonist-antagonist analgesic synthesized in 1965. It is structurally related to the pure agonist oxymorphone and the pure antagonist naloxone.

**Pharmacokinetics:**

**Mechanism of Action:**

Nalbuphine binds readily to both mu – and kappa receptor.

Action on mu – receptor has Antagonist effects.

Action on kappa – receptor has Agonist effects which produces analgesia.

**Dosage**:

Maximum single dose : 20mg / dose

Maximum total daily dose : 160 mg/day

**Absorption:**

Nalbuphine administered parentrally (intramuscular/intravenous/ subcutaneous)

**Onset and Duration**

**Onset**

Intravenous : within 2 – 3 minutes

Intramuscular and subcutaneous: Less than 15 minutes

**Duration:**

Single dose : 3 to 6 hours

**Time to peak concentration:**

Intravenous : Peak effects seen within 30 minutes

Intramuscular: 0.48 to 0.63 hour

Subcutaneous: 0.44 to 0.48 hour

**Distribution:**

Nalbuphine is not bound to plasma protein.

Nalbuphine crosses the placenta.

**Metabolism**

It undergoes hepatic metabolism to pharmacologically inactive conjugates. Both unchanged drug and conjugates are secreted into bile.

**Excretion**

Major route of elimination is fecal with little renal elimination (7%)

**Indication:**

Relief of moderate to severe pain.

Preoperative and post operative analgesia.

Supplement to balanced anaesthesia.

**Administration:**

Recommended dose: 10mg/ 70 kg adult can be administered IV/IM/SC. Dosage should be administered according to severity of pain, physical status of patients & other medications.

**Cautions:**

**A) Contraindications:**

Hypersensitive to Nalbuphine or any ingredients of the preparation.

**B) Precautions:**

Impaired respiration – (Bronchial Asthma)

Impaired renal / hepatic function

Myocardial infarction

Coma, head injury, intracranial lesion, or increased intracranial pressure.

**PHARMACODYNAMIC ACTION**

The safety and efficacy of nalbuphine as an analgesic for the management of moderate to sever pain have been documented by several studies. In chronic pain studies with orthopedic and cancer patients, the analgesic effect of nalbuphine is comparable with that of morphine on a milligram to milligram basis without overt evidence of development of physical tolerance.

Use of nalbuphine in acute postoperative pain indicates that the drug is equipotent to or only slightly less potent, than morphine. As preoperative medication nalbuphine and morphine in doses of 0.1 and 0.15 mg kg-1 respectively, are equianalgesic. In analgesic supplemented (balanced) anaesthesia, nalbuphine offers several advantages over morphine –

1. Cardiovascular stability.
2. Adequate postoperative ventilation
3. Rapid recovery of wakefulness.
4. lower incidence of nausea and vomiting.
5. Shorter stay in the recovery room.

Mean total dose requirements are usually 1mg-kg-1 (compared with 0.5 mg.kg-1 morphine) with a range of 0.5 to 3mg.kg-1. Parenteral nalbuphine is also effective in pain relief during labour, acute MI and a variety of medical conditions including renal and biliary colic.

Nalbuphine in doses of 10 mg per 70 kg causes respiratory depression approximately equal to that produced by a similar dose of morphine, but in contrast to morphine, respiratory depression is not appreciably increased with higher doses of nalbuphine. Respiratory depression peaks or plateau at about 30 mg/70 kg with adequate post operative ventilation, following the intraoperative use of as high as 3mg.kg-1. Naloxone effectively reverses the respiratory depression but is rarely required.

IV nalbuphine is associated with hemodynamic stability when used for cardiac catheterization, acute myocardial infarction and

intraopertively. A stable circulation may be partly related to minimal histamine release by this agent. This is in contrast to morphine which liberates measurable amounts of histamine. The hemodynamic effects of nalbuphine differ from those of pentazoine and butorphanol which increase pulmonary artery pressure and cardiac work load.

Chronic administration of nalbuphine produces a physical dependence which resembles that of pentazocine, since it has elements of both morphine and nalorphine dependence. Nalbuphine will not substitute for morphine in narcotic depedent individuals and in fact will precipitate abstinence. Studies indicate that nalbuphine has a relatively low abuse potential. Nalbuphine is not subject to narcotic control.

Nalbuphine may cause miosis which usually occur after the first dose. In one study it was found that nalbuphine was about one quarter as potent as nalorphine as an antagonist in subjects dependent on 60 mg of morphine a day. It has also been used to reverse narcotic induced respiratory depression without reversing analgesia. Nalbuphine has no effect on the ECG, little effect on the EEG and no major effect on clinical laboratory test values.

**Adverse Effects:**

- 10% CNS: Fatique, drowsiness, headache, dizzness, night mares,
- 1% to 10%: Histamine release
- CVS: Hypotension
- GIT: Anorexia, Nausea, Vomiting, dry mouth
- Local: Pain at the injection site
- Neuromuscular/Skeletal: Weakness
- < 1% bradycardia, tachycardia, pulmonary oedema, narcotic Neuromuscular/Skeletal: Weakness
- < 1% bradycardia, tachycardia, pulmonary oedema, narcotic withdrawal.

The drug should be used with caution in emotionally unstable persons, those with a history of narcotic abuse, patients with head injury or elevated intracranial pressures and in the presence of ventilatory renal or hepatic dysfunction. Nalbuphine dosage should be reduced when other central nervous system

depressant drugs are administered. It has not been extensively studied in children, pregnant women or during labour and delivery.

Oral nalbuphine (not yet commercially available) is about one-third as potent as intramuscular nalbuphine. As an analgesic supplement to balanced anesthesia, doses range from 0.5 to 3mg.kg-1 with an average dose of 1 mg.kg-1.

## BUPIVACAINE

Bupivacaine was synthesized in 1957 by Ekenstam and his colleagues and used clinically by Telivuo in 1963.

**PHARMOKINETICS**

It is a N-butyl pipecolic. 2,6 dimethyl xylidide hydrochloride

Molecular Weight 288

PKA 8.05 – 8.1.

Partition coefficient 27.5

Proteing Binding 95%

Specific gravity at $37^{o}c = 0.998$.

It is highly lipid soluble and has a potency of approximately four times that of lignocaine and mepivacaine. It is more protein bound and less cumulative. It has a longer latency and a longer

duration of action. It appears to produce sensory analgesia more efficiently than motor block.

Metabolism: After systemic absorption, the drug is metabolized in the liver by N-dealkylation to pipecoly xylidine (ppx) which is approximately one eights as toxic as bupivacaine. PPX and unchanged bupivacaine are excreted in equal proportions in the urine. The slow phase half life (t ) is about eight hours in the normal subjects.

Toxic level: Scott (1975) suggests that a venous concentration of 2ug/ml gives rise to toxic effects when the drug is administered rapidly.

**Mechanism of Action:**

1. Bupivacaine acts directly on the receptors within the sodium channels of the nerve membrane.
2. Produces non-specific membrane expansion.

Pharmacological effects

a) Local: Nerve Blockade

b) Regional: Pain, temperature, touch, motor power

and vasomotor tone in the region supplied by the nerves are blocked.

c) Systemic: Effects occurring as a result of systemic absorption.

**Pharmodynamics**

**i) CVS: Dose related**

Heart: Depresses automaticity, myocardial contractility and reduces cardiac sensitivity to adrenaline.

Gross overdosage produces ventricular tachycardia, fibrillation and cardiac arrest.

ii) CNS: Sedation, light headedness, anxiety and restlessness

Toxicity: Circumoral numbness paraesthesia, twitching, visual disturbances, convulsions coma, respiratory and cardiac depression.

iii) Neuromascular junction:

Blocks motor nerves and presynaptic junction.

iv) Hypersensitivity reaction: Rare.

Preparations available:

Epidural:

1. 0.125% - pain relief, high failure rate, brief duration

2. 0.25% only sensory blockade, motor blockade poor
3. 0.5% successful sensory blockade with minimal motor blockade.
4. 0.75% adequate motor and sensory blockade.

Spinal

Hyperbaric: 0.5% & 0.75%

Isobaric: 0.5%

Maximal Dose:2mg/kg.

Carbonation and alkalinization:

Most of the clinically used adjuvants alter the physiochemical properties of local anaesthetics. Of this, one of them is adjusting the pH of local anaesthetic, by addition of sodium bicarbonate or the use of carbonated local anaesthetics.

It is the lipid soluble undissociated base form of the drug that penetrates the neural membrance to reach the interior of the axoplasm ( Ritchie et al).35 The pharmacologic effect, blockade of nerve conduction, however, is produced by the water soluble dissociated cationic form. The degree of dissociation is determined

by the Henderson – Hasselbach equation and is dependent on the drug's dissociation constant (pKa).

The pKa of commonly used local anaesthetics is between 7.7 and 8.9. Lignocaine and Bupicaine have a pKa of 7.9 and 8.1 respectively. Most of the commercial preparations of local anaesthetics are quite acidic ( pH ranging from 4.2 -6.5) to improve stability of the drug and thus prolong its shelf life. At this range of pH, less drug is available in the undissociated base form, which is required to transfer across the perineural sheath and neural membrane. Agents influencing the degree of dissociation should therefore have an effect on the onset and degree of neural blockade.

However upward adjustment of pH should be done very carefully as excessive alkalinization causes the local anaesthetic to precipitate. This is especially common with bupivacaine and etidocaine.

# REVIEW OF LITERATURE

**1.Romagnoli A. Keeats As 1980**

Studied the ceiling effect for respiratory depression by Nalbuphine and morphine and demonstrated that with higher doses of morphine respiratory impairment progress to apnoea, where as with nalbuphine did not apnoea occur demonstrating the reversal effect.

**2. Dondoni R,Rolly G,Devulder J,Verdonck R,Acta Anaesthesiol Belg 1988;39(4):251-6**

Compared Nalbuphine 20gm I.M. to pentazocine 30 mg I.M. for postoperative pain relief after orthopedic surgery.Onset duration and quality of pain relief were significantly superior for nalbuphine with 50% of the obseravation period. Cardiovascular and side effect were in both group minor.

**3. van den Berg AA, Honjol NM, Prabhu NV,Datta S, Rozario CJ, Muarleedaran R,Savva D. Department of Anaestheesia,Riyadh Armed Forces Hospital,Kingdom of Saudi Arabia. Br J Clin Pharmacol 1994 Dec; 38 (6) : 533-43**

To rationalize the choice of analgesic for routine ENT

surgery they examined the intraoperative, recovery and postperative effect following the administration of ethier buprenorphine (3.0 to 4.5 microgrms Kg-1), diclofenac(1 mg Kg-1), fentnyl(1.5 to 2.0 microgrms Kg-1), morphine(0.1 o 0.15 mg Kg-1), nalbuphine(0.1 to 0.15 mg Kg-1), pethidine(1.0 to 1.5 mg Kg-1), or saline(as control) given with the induction of anaesthesia in 374 patients.Intraoperatively their effecs on heart rate and blood pressure, airway pressure and intraocular pressure, were similar. Nalbuphine and pehidine produced sedation with analgesia during recovery, a prolong time to re-medication and mild emeic effect.

**4. Jeon SY,Lee SH, kwon BY, Koren J anesthesiol.1996 Dec;31(6):764-770. Korean.**

Described the usefullness of the epidural injection of narcotics for the relief of postoperative pain. Morphine, a u-receptor agonist, produce strong analgesic effect with some side effect.Nalbuphine, is a mu-antagonist and kappa-agonist, has an anlagesic effect comparable to morphine with little side effect.Nalbuphine hydrochloride could be better agent then morphine in term of complictation.

**5. Khan FA, Zaidi A, kamal RS.**

**Anaesthesia.1997 Nov;52(11):1095-101.**

Evaluated the efficacy of Nalbuphhine and Buprenorphine in total intravenous anaesthesia. No difference was observed in blood pressure but the heart rate was significantly lower in the buprenorphine group. intra-operative bradycardia(heart rate<60 beat.min-1) occurred more often in the buprenorphine group. Recovery was fast and comparable with both drugs and no patient reported awareness. Quality of analgesia was similar in both groups. Both drugs provide suitable analgesic supplementation and nalbuphine offers useful alternative to buprenorphine .

**6. Parker et l,1997.**

Assessed the analgesic effect of Nalbuphine with hydromorphone in post caesarean delivery.In a double bliend trial, 78 women were given hydromorphone 0.075 mg/ml alone or with nalbuphine 0.02,0.04, or 0.08 mg/ml.

A mixture of hydromorphone and nalbuphine provided more effective PATIENT-CONTROLLED EPIDURAL ANALGESI

with fewer side effects than hydromorphone alone for women recovering from caesarean delivery. Nalbuphine produced dose-dependent decrease in urinary retention, itching, nausea and some of the typical opioid side effects were greatly reduced.

**7. Anesth Anlg 1999;88:686**

compared Nalbuphine, Meperidine, and placebo for treating Postanesthetic Shivering. Ninety adult patients included in the study. Group 1received IV nalbuphine 0.08mg/kg, Group 2 received IV mepridine 0.4mg/kg, and Group 3 received IV saline. Treatment that stopped shivering was considered to have been successful. Results demonstrated that both nalbuphine and meperidine provide a similar rapid and potent anti-shivering effect. Nalbuphine may be an alternative to meperidine for treating postanesthetic shivering

**8 .Khlid Maudood Siddiqui,Ursula Chohan (JPMA 57:67;2007).**

Compared the result of tramadol with Nalbuphine for dilatation and evacuation with total intra-venous anaesthesia technique. A total of 70 patients where included in this prospective, double blind randomized study. Intravenous tramadol 1.5mg/kg and

nalbuphine 0.1mg/kg where compared in total intravenous anaesthesia using a propofol infusion in patients undergoing dilataion and evacuation Change in haemodynamic variables greater then 20% from the base line values were noted. Quality of analgesia was better in nalbuphine group but both drugs provided suitable analgesic supplementation .

**9.Brock-Utne JG, Ritchie P,Downing JW.**

Compared the efficacy and impact on respiratory rate of Nalbuphine and pethidine used for postoperative pain relief. Nalbuphine hydrochloride, a synthetic agonist-antagonist analgesic, in a dose of 20mg was compared with pethidine 100mg in 60 patients after elective surgery in a random double-blind study. Both drugs were given intramuscularly on the first day after surgery The result of study shown that nalbuphine had a long duration of action. There was significant respiratory depression with pethidine group.

**10.Tammisto T, Tigerstedt I.**

Compared the analgesic effect of Nalbuphine and pentazocine during the immediate post operative period after

abdominal surgery. The onse of pain relief was similar and the peak effect occurred about half an hour after the injection both drugs. On a milligram basis, Nalbuphine seemed to be about three times as potent as pentazocine. The duration of action seemed to be slightly longer after nalbuphine, but 2 1/2hrs. after the injection the pain had returned to pre injection level in 2/3 of the patients, even after the higher doses of both drugs. Except for sleepiness, there were few side effect and they were similar after both drugs. No psychotomimetic effects were observed.

**11.Hook PC, lvery KM.**

Compared the effect and safety to Nalbuphine and Pentazocine with midazolam in patients undergoing minor oral surgery under local analgesia. Forty patients, aged between 17 and 48 years and A.S.A.Class I prticipated. The results confirmed that the use of either nalbuphine(0.2 mg/kg) or pentazocine(0.5 mg/kg) allowed for a significant reduction in the mean dosage of midazolam required to produce satisfactory sedation when compared with trials, where midazolam was used alone. Inadvertent overdosage with midazolm is prevented as the onset of sedation and its end-point are more obvious.

**12. Van den Berg AA, Montoya – Pelaez LF, Halliday EM, Hassan I, Baloch MS Department of Anesthesia, Riyadh, Kingdom of Saudi Arabia.**

Compared the perioperative analgesic and recovery characteristics of equipotent doses of tramadol, pethidine and nalbuphine(3.0 mg kg-1 nd 0.3 mg kg-1 respectively) with placebo(saline0.02 ml kg-1)given at induction of anaesthesia.

Equipotent dose of tramadol, pethidine and nalbuphine (3.0 mg kg-1,1.5mg kg-1 and 0.3 mg kg-1 respectively) with placebo (saline 0.02 ml kg-1) given t induction of anaesthesia in 152 ASA. 1 children and young adults undergoing tonsillo-adenoidectomy. Pethidine and nalbuphine reduced the intra-operative esmolol requirement more significantly ($p < 0.025$ and $p < 0.005$ respectively) and the need for need for treatment during recovery was only opioids ($p < 0.005$each). These results suggest that pethidine 1.5 mg/kg and nalbuphine 0.3 mg/kg given with induction of anaesthesia provide better analgesia during and after tonsilloadenoidectomy than does tramadol 3.0mg/kg.he the time to recovery was delay with pethidine suggests a greater safety profile of nalbuphine and tramadol.

# MATERIALS AND METHODS

This study was done at Govt. Rajaji Hospital Madurai. 100 patients belonged to ASA grade I & II with age of 20-60 years underwent elective infra umbilical surgeries were chosen.

**Exclusion Criteria:**

- Patients with spinal deformities,
- Local skin sepsis,
- Bleeding disorders and
- Psychiatric illness

Informed consent obtained after explaining the procedure. Preanaesthetic assessment done to find out systemic illness complicating anaesthesia.

**Premedication:** inj. atropine 0.02mg/kg given 45minutes prior to surgery. No narcotic premedication. The patients were explained about the 10 point visual analogue of pain scale. The patients were randomly chosen into two groups.

**Group A:**

Received 15 ml of 0.5% bupivacaine with nalbuphine 10mg.

**Group B:**

Received 15 ml of 0.5% bupivacaine alone.

The following equipment's kept ready before administering epidural anaesthesia.

Boyles machine with 02 source.

Working Laryngoscope and appropriate size ET tubes.

Suctioning apparatus,

Vasopressors.

All emergency drugs.

**TECHNIQUE**

An intravenous line with dextrose normal saline started. Base line recording of pulse rate, blood pressure, respiratory rate and oxygen saturation noted down. Patients were placed in the right lateral position on a horizontal table with head supported by a pillow.

**Contents of epidural tray:**

- Sponge holding forceps
- Sterile gauze pieces
- Bowl with antiseptic solutions
- Sterile towels
- 5ml syringe with 24 G-needle
- 16 G-huber point Tuohy needle
- 10ml glass syringe with freely moving piston

- 1ml insulin syringe
- Nalbuphine ampoule
- Sterile water for injection
- 0.5% bubivacaine vial

After thorough aseptic precaution L1-L2 or L2-L3 Space located and using a 16 gauge Huber point Tuohy needle epidural space was identified with loss of resistance technique. Epidural catheter was inserted and fixed.

Aspiration was done to rule out subarachnoid or intravascular placement of the catheter. A test dose of 2 ml of 1% lignocaine with 10 microgram of adrenaline was injected through the catheter and finally the total dose of 15 ml of 0.5% bupivacine with injection nalbuphine was injected through the catheter and the patients were positioned for the surgery.

The level of sensory blockade was assessed every 2minutes. The time taken for level of block at T10 and the maximum time for maximum level of block noted down. The time taken for grade 3 motor block noted down. Surgeons asked to proceeded the surgery only after the maximum level of blockade was established. The 2 segment regression time was noted. The pulse rate, blood pressure,

respiratory rate were monitored every 5minutes. Continuous oxygen saturation monitoring done. A fall in systolic blood pressure by 20% from the base line value was considered as hypotension and managed with IV fluids, oxygen and inj. Ephedrine in incremental doses. At end of surgery patients were observed in the recovery room for further two hours and sent to postoperative ward. The level of consciousness assessed ever ½ hour and graded according to the sedation score.

Patients were asked to mark a point scale on the 10 point visual analogue scale of pain according to the intensity of pain. The observation was done every 30 minutes. The pain relief is graded according to VAPS as follows.

| **VAPS** | **Quality of analgesia** |
|---|---|
| 0-1 | Excellent |
| 1-4 | fair |
| 4-6 | good |
| 6-8 | slight |
| 8-10 | no relief |

## DURATION OF ANALGESIA

The duration of analgesia was taken as the period from the time of giving epidural analgesia till the patient's first requirement of systemic analgesic medication. Supplementary analgesia was given when VAPS more than 6.

## SEDATION SCORE LEVEL

The level of sedation assessed every 30minutes and graded according to the sedation score. (Brain and Ready)

0- fully awake

1- Normal sleep

2- Drowsy, arousable on touch

3- Drowsy arousable to painful stimuli

4- Somnolent.

The side effects due to Nalbuphine like nausea, vomiting, pruritis, urinary retention were noted down. Comparison between group A and group B were done using students 't' test and the level of significance was taken below 0.05.

# RESULTS

## VARIABLES AFFECTING COMPARABILITY BETWEEN THE STUDY GROUPS

### 1. Age and Duration of the procedure among the Study Groups

| Study groups | | N | Mean | S.D | S.E | T- Test (p Value) |
|---|---|---|---|---|---|---|
| Age of the patient | Study group (Bupi+ Nalbu) | 50 | 43.26 | 7.645 | 1.081 | 0.974 |
| | Control (Bupi) | 50 | 43.20 | 10.768 | 1.523 | |

### 1a. Age Distribution of Study Population

| Study groups | | Frequency | Percent | X2 Test (p value) |
|---|---|---|---|---|
| **Study group (Bupi+ Nalbu)** | 20- 30 yrs | 4 | 8.0 | 0.792 |
| | 30- 40 yrs | 13 | 26.0 | |
| | 40- 50 yrs | 25 | 50.0 | |
| | 50- 60 yrs | 8 | 16.0 | |
| | Total | **50** | **100.0** | |
| **Control (Bupi)** | 20- 30 yrs | 8 | 16.0 | |
| | 30- 40 yrs | 12 | 24.0 | |
| | 40- 50 yrs | 19 | 38.0 | |
| | 50- 60 yrs | 10 | 20.0 | |
| | >60 yrs | 1 | 2.0 | |
| | Total | **50** | **100.0** | |

## 2. Surgeries Performed among the Groups

| Study groups | | Frequency | Percent |
|---|---|---|---|
| Study group (Bupi+ Nalbu) | TVH | 5 | 10.0 |
| | Herniatomy/raphy | 18 | 36.0 |
| | Varicose Veins | 13 | 26.0 |
| | Appendicectomy | 11 | 22.0 |
| | Below knee amputation | 1 | 2.0 |
| | SSG | 2 | 4.0 |
| | Total | 50 | 100.0 |
| Control (Bupi) | TVH | 4 | 8.0 |
| | Herniatomy/raphy | 22 | 44.0 |
| | Varicose Veins | 9 | 18.0 |
| | Appendicectomy | 11 | 22.0 |
| | Below knee amputation | 3 | 6.0 |
| | SSG | 1 | 2.0 |
| | Total | 50 | 100.0 |

Chi Square Test: p Value=0.766

### 3. Group Statistics

| Study groups | | N | Mean | S.D | S.E | Independent T-Test (p Value) |
|---|---|---|---|---|---|---|
| Duration of procedure | Study group (Bupi+ Nalbu) | 50 | 61.48 | 7.538 | 1.066 | 0.273 |
| | Control (Bupi) | 50 | 63.00 | 6.171 | .873 | |
| Baseline Systolic BP | Study group (Bupi+ Nalbu) | 50 | 118.12 | 16.529 | 2.338 | 0.276 |
| | Control (Bupi) | 50 | 121.32 | 12.353 | 1.747 | |
| Baseline Pulse Rate(5min) | Study group (Bupi+ Nalbu) | 50 | 80.56 | 6.276 | .888 | 0.858 |
| | Control (Bupi) | 50 | 80.34 | 6.022 | .852 | |

### 4. Variability of the Study characters

| | | N | Mean | S.D | S.E | Independent T Test (p Value) |
|---|---|---|---|---|---|---|
| Time of onset of block | Study group (Bupi+ Nalbu) | 50 | 5.22 | 1.234 | .174 | 0.000 |
| | Control (Bupi) | 50 | 9.52 | 1.446 | .205 | |
| Onset of Grade III motor block | Study group (Bupi+ Nalbu) | 50 | 7.80 | 1.471 | .208 | 0.000 |
| | Control (Bupi) | 50 | 12.84 | 1.390 | .197 | |
| Two segment regression time | Study group (Bupi+ Nalbu) | 50 | 70.14 | 6.138 | .868 | 0.009 |
| | Control (Bupi) | 50 | 67.00 | 5.544 | .784 | |
| Duration of Analgesia | Study group (Bupi+ Nalbu) | 50 | 287.40 | 29.054 | 4.109 | 0.000 |
| | Control (Bupi) | 50 | 37.64 | 18.307 | 2.589 | |
| Visual analogue score | Study group (Bupi+ Nalbu) | 50 | 1.86 | .756 | .107 | 0.000 |
| | Control (Bupi) | 50 | 7.22 | 1.447 | .205 | |
| Sedation score | Study group (Bupi+ Nalbu) | 50 | 0.46 | 0.503 | 0.071 | 0.000 |
| | Control (Bupi) | 50 | 0 | 0 | 0 | |

## 5. Respiratory Rate And Oxygen Saturation Change during the Procedure

| Study groups | | N | Mean | S.D | S.E | Independent T-Test (p Value) |
|---|---|---|---|---|---|---|
| Respiratory rate | Study group (Bupi+ Nalbu) | 50 | 14.08 | .877 | .124 | 0.362 |
| | Control (Bupi) | 50 | 14.24 | .870 | .123 | |
| Oxygen saturation | Study group (Bupi+ Nalbu) | 50 | 98.80 | .881 | .125 | 0.000 |
| | Control (Bupi) | 50 | 97.28 | .904 | .128 | |

## 6. Systolic Blood Pressure Variability During The Procedure

| | Systolic BP (5min) | | Systolic BP (15min) | | Systolic BP (30min) | | Systolic BP (45min) | |
|---|---|---|---|---|---|---|---|---|
| | Study group (Bupi+ Nalbu) | Control (Bupi) | Study group (Bupi+ Nalbu) | Control (Bupi) | Study group (Bupi+ Nalbu) | Control (Bupi) | Study group (Bupi+ Nalbu) | Control (Bupi) |
| N | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 |
| Mean | 118.12 | 121.32 | 114.84 | 100.40 | 111.96 | 113.54 | 112.72 | 120.86 |
| Std. Deviation | 16.529 | 12.353 | 11.809 | 11.249 | 9.454 | 13.852 | 9.439 | 12.746 |
| S.E | 2.338 | 1.747 | 1.670 | 1.591 | 1.337 | 1.959 | 1.335 | 1.802 |
| Independent T-test (p Val) | 0.276 | | 0.000 | | 0.507 | | 0.000 | |

## 7. Pulse Rate Variability During The Procedure

| | Pulse Rate (5min) | | Pulse Rate (15min) | | Pulse Rate (30min) | | Pulse Rate (45min) | |
|---|---|---|---|---|---|---|---|---|
| | Study group (Bupi+ Nalbu) | Control (Bupi) | Study group (Bupi+ Nalbu) | Control (Bupi) | Study group (Bupi+ Nalbu) | Control (Bupi) | Study group (Bupi+ Nalbu) | Control (Bupi) |
| N | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 |
| Mean | 80.56 | 80.34 | 74.38 | 89.04 | 72.40 | 91.98 | 72.22 | 92.32 |
| S.D | 6.276 | 6.022 | 5.893 | 7.640 | 5.753 | 6.862 | 5.486 | 6.844 |
| S.E | .888 | .852 | .833 | 1.080 | .814 | .970 | .776 | .968 |
| Independent T-test (p Val) | 0.858 | | 0.000 | | 0.000 | | 0.000 | |

**Complications**

| Study groups | | | Frequency | Percent |
|---|---|---|---|---|
| Study group (Bupivacaine+ Nalbuphine) | Valid | Absent | 50 | 100.0 |
| Control (Bupivacaine) | Valid | Absent | 38 | 76.0 |
| | | Hypotension | 11 | 22.0 |
| | | Vomitting | 1 | 2.0 |
| | | Total | 50 | 100.0 |

**Visual analogue score**

| Study groups | | | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|---|---|
| Study group (Bupivacaine+ Nalbuphine) | Valid | 1 | 18 | 36.0 | 36.0 | 36.0 |
| | | 2 | 21 | 42.0 | 42.0 | 78.0 |
| | | 3 | 11 | 22.0 | 22.0 | 100.0 |
| | | Total | 50 | 100.0 | 100.0 | |
| Control (Bupivacaine) | Valid | 4 | 1 | 2.0 | 2.0 | 2.0 |
| | | 5 | 6 | 12.0 | 12.0 | 14.0 |
| | | 6 | 11 | 22.0 | 22.0 | 36.0 |
| | | 7 | 7 | 14.0 | 14.0 | 50.0 |
| | | 8 | 13 | 26.0 | 26.0 | 76.0 |
| | | 9 | 12 | 24.0 | 24.0 | 100.0 |
| | | Total | 50 | 100.0 | 100.0 | |

## OBSERVATION AND RESULTS

Patients in both groups were comparable in age, duration, the site and type of surgery and baseline parameters at the starting of procedure. (Table 1,2,&3). The observation recorded in this study are given as follows.

**Results of Study characters and baseline measurement.**

**Age:** Group A: The mean of 43.26

Group B: The mean of 43.20

't' test (p value) 0.974

Age distribution : t test is 0.792

Surgery performed : 0.766 (chi-square)

| Duration of procedure : | Group A | B | t |
|---|---|---|---|
| | 61.48 | 63 | 0.273 |
| Systolic BP | 118.12 | 121.32 | 0.276 |
| Pulse Rate | 80.56 | 80.34 | 0.858 |

< 0.05 insignificant

There were statistically no significant difference between mean age distribution, surgery performed duration of procedure and baseline parameters in both groups.

## RESULTS OF VARIABLES OF STUDY CHARACTERS BETWEEN 2 GROUPS

The significance between the study and control groups was tested using the standard error of difference between the means

### TIME OF ONSET OF SENSORY BLOCK (Table. 4)

In group A the minimum time was 3 minutes and maximum 8 minutes with a mean time of 5.22.

In group B the minimum time was 6 minutes and maximum 12 minutes with a mean time of 9.52 minutes.

R. Fournier, et al. Oct 1998 studied and reported the administration of intrathecal nalbuphine resulting in a significantly faster onset related with the time to the lowest pain score ($18 \pm 11$ VS $66 \pm 75$ minutes, $P < 0.001$)

In the study also rapid onset in group A patients is due to synergistic effect of nalbuphine and bupivacaine.

### TIME OF ONSET OF MOTOR BLOCK(Grade 3)

All patients both groups developed Grade 3 Motor Block. The time latency for complete blockade was taken as the onset of motor block.

In group A the minimum time was 5 minutes and maximum 10 minutes with a mean time of 7.8.

In group B the minimum time was 9 minutes and maximum 15 minutes with a mean time of 12.84 minutes.

Since actual difference between the mean is 5.04 – the study is significant ($P < 0.000$)

**2 SEGMENT REGRESSION TIME (Table 4)**

In the group A the regression time was the range of 60-83 minutes with mean of 70.14.

In the group A the regression time was the range of 54-84 minutes with mean of 67 with $P < 0.009$ which is significant.

**QUALITY OF ANALGESIA**

The minimum VAPS was 1 and maximum 3 in Group A in the mean of 1.86.

In group B the quality of analgesia was not assessed since all of them received postoperative narcotic supplementation after the surgery.

In group A the quality of analgesia was fair in 30 (85.7%) patients and good in 5 (14.3%).

Supported by the study of Donadoni R. et al 1988 in which concluded that nalbuphine was far superior in onset duration and quality of pain relief in orthopaedic surgeries when compared to pethidine.

**DURATION OF SURGERY**

In Group A the mean duration of surgery was 61.48 minutes, and 63 minutes in Group B. t value is 0.27.

**SEDATION**

In Group A 23 patients had sleep resembling natural sleep with sedation score of and 27 patients with sedation score of 1 with the mean of 0.46 (p value 0.000) which is statically significant.

In Group B all patients were awake.

KC 1983 studied the role of epidural analgesic and sedatives in the management of pain and agitation in which he compared nalbuphine with other narcotics.

**RESPIRATORY RATE**

Respiratory rate< 10/ minute was not noted in any of patients.

**OXYGEN SATURATION**

Measured by pulse oximetry was maintained above 95% in all patients.

Group A 98.8

Group B 97.2

t test (p value is 0.000) which is significant

**CHANGES BLOOD PRESSURE.**

| Time in minutes | Group A | Group B | t value |
|---|---|---|---|
| 5 | 118.12 | 100.4 | 0.276 |
| 15 | 114.84 | 100.4 | 0.000 |
| 30 | 119.6 | 113.54 | 0.05 |
| 45 | 112.72 | 120.86 | 0.000 |

There is significance in BP maintenance in group A throughout the procedure where as in group B it falls below the base line value after 5 minutes and 15 minutes and then raises after 30 min and 45 minutes.

**CHANGES PULSE RATE**.

| Time in minutes | Group A | Group B | t value |
|---|---|---|---|
| 5 | 80.6 | 80.3 | 0.8 |
| 15 | 74 | 89 | 0.000 |
| 30 | 72 | 92 | 0.000 |
| 45 | 72 | 92 | 0.000 |

No Hypotension occurred in group A and in group B 11 patients have hypotension. In contrast to pentazocine and butorphanol, nalbuphine does not increase systolic blood pressure and pulmonary arterial pressure, heart rate (or) atrial filling pressure (Lee et al; 1976)

**SIDE EFFECTS**

NAUSEA AND VOMITING occurred in 1 patient in group B.

URINARY RETENTION could not be studied as the patients were catheterized at the end of surgery.

Parker et al studied the interaction between nalbuphine and hydromorphone and concluded that the combination of hydromorphone 0.075 mg/ml and nalbuphine 0.04mg/ml resulted in lower nausea score and decreased incidence of urinary retention compared with hydromorphone alone.

PRURITIS: No patient has pruritis in the post operative period in group A and in group B.

DROWSINESS: In group A no patients had sedation score of more than one. In group 'B' all the patients were awake.

RESPIRATORY DEPRESSION: did not occur in any of the patients.

Nalbuphine 10 to 20mg reverses postoperative ventilation caused by fentanyl but maintain analgesia (Bailey et al 1987; molden Hawer et al, 1985)

Depression of ventilation is similar to that of morphine until 30mg of nalbuphine is exceeded, after with no further depression of ventilation occurs (ceiling effect) (Gal et al; 1982)

# DISCUSSION

Epidural administration of narcotics for post surgical analgesia is becoming increasingly popular with more practitioners. This is clearly because this modality of analgesia has unique advantages over conventional, intermittent IV/IM administration of narcotics. Patients given epidural narcotics have fewer respiratory complications and can be mobilized sooner in the postoperative period.

However, the drug that has been utilized most widely, i.e., morphine, produces distressing side effect and sometimes potentially lethal complications like delayed and prolonged respiratory depression*. several other narcotics have been evaluated in order to identify a drug that affords as efficient analgesia but causes much less respiratory depression when given epidurally for epidural use. The agonist/antagonist narcotic agent can be expected to offer some scope in this respect, since the respiratory depression reaches ceiling level* with higher receptor occupancy at higher dose of the drug. Apart from this these drugs are not as potent as morphine in causing respiratory depression*. In this study, neither bradypnoea nor frank respiratory depression was encountered.

The agonist – antagonist class of drugs have the advantage that they trend to release less histamine and thus cause less hypotension.

Similarly, they also have less abuse potential. Thus nalbuphine being an agonist antagonist has all these advantages.

Epidurally administered nalbuphine reported satisfactory outcome with regard to quality of analgesia and incidence of serious complications*. In the present study also there was no respiratory depression and nausea and vomiting, however PaCO2 level were not monitored.

The quality of analgesia was good in patients given epidural nalbuphine. At the end of any period of observation, more patients from group A had zero points on the VAS as compared to those from Group B. It was found that none of the Group B patients had zero pain score after 24 hrs. This could be because epidurally given nalbuphine could no longer provide pain relief after 24 hrs. While those in Group B could have demanded and obtained analgesia shortly before pain score was measured.

No troublesome side effect were encountered either in the experimental or in the control group .Some patients in Group A were very drowsy. After allowing them to sleep for half an hour, they were sufficiently awake to use the visual analog scale. None required catheterization of the urinary bladder. None experienced itching,

vomiting, shivering , although other studies have reported these with extradural fentanyl, dimorphine and other opiates*.

It was one of the explicit aims in the present study to measure the duration of analgesia in the epidural group, It was observed that patients demanded analgesia at the end of 7 hours (5.5 mean). In the study by Weksler et al epidural nalbuphine provided a mean duration of analagesia for 8 hrs and 45 min(±2.25 hrs)*.

# SUMMARY

In this study, epidural NALBUPHINE was evaluated as an analgesic and its influence on BP, PR, oxygen saturation. Fifty adult patients undergoing infra umbilical surgery electively were included in the study. All were fit patients belonging to ASA category I/II. Fifty patients who were matched for age, type of surgery, duration of surgery and baseline parameters received analgesia according to the stranded protocol. They were control groups. Injection into epidural space in the study group was given before starting of surgery. Pain was measured on a visual analogue scale and PR, oxygen saturation by pulse oxymetry.

When nalbuphine given epidurally has provided excellent analgesia in the immediate intraoperative and postoperative period. As reported in several studies Nalbuphine offered good cardiovascular stability without the risk of several respiratory depression though it produce sedation in some of our patients. Our patients had good overall analgesia with improved respiratory function.

Nalbuphine when used with Bupivacaine decrease the onset time of sensory blockade and time taken for grade3 motor block. It produces post operative analgesia for period of 4- 7 hours with a mean duration of 5.5 hours.

No incidence of nausea, vomiting, shivering were noted with epidural nalbuphine.

Nalbuphine when combined with Bupivacaine hastens the onset of sensory block. It is speculated that, with studies invoking larger sample of patients, nalbuphine may well emerges an alternative to other opoids for epidural use.

# CONCLUSION

This prospective, randomized, single blind study , wherein Nalbuphine in a dose of 10 mg was added epidurally to 0.5% Bupivacaine – for infra umbilical surgeries concludes that

" epidural Nalbuphine hastens the onset of both sensory and motor blockade and significantly prolonged the duration of anaesthesia and postoperative analgesia, with stable haemodynamics"

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## PROFORMA

Name : Age / Sex : IP No. :

Address :

Diagnosis : Surgery : DOA : Unit :

Anaesthesiologist : Surgeon :

Pre Anaesthetic Assessment

General Condition

Weight

CVS

RS

PR

BP

Spines

Airway

ASA status

Preoperative Investigations

Urine Albumin

Sugar

Hb%

BT

CT

Blood Urea

Blood sugar

Serum creatinine

Blood grouping

Chest X ray

ECG

**Premedication**

Drug Dose Route Time

Technique of Anaesthesia : Lumbar epidural

Position : Right lateral Space : L1 – L2 Approach : Midline

Needle : 16 G Catheter : 10 cm Drug : Bubivacaine 0.5%(15ml)

Time of Admission : Time of Onset : Sensory level :

Time of two segment regression :

Total duration of Surgery

Grade I Motor block

Motor level (Modified Bromage scale)

(0- No motor loss, 1 – Inability to flex hip 2 – Inability to flex the knee 3 – Inability to flex the ankle)

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Time | | | | | | | | | |
| Level | | | | | | | | | |

Sedation score (Three point ordinal scale)

(0- awake, 1 – Drowsy but arousal, 2 – sleeping, 3 – unarousable, 5 – No response to loud voice, 6 – No response to pain)

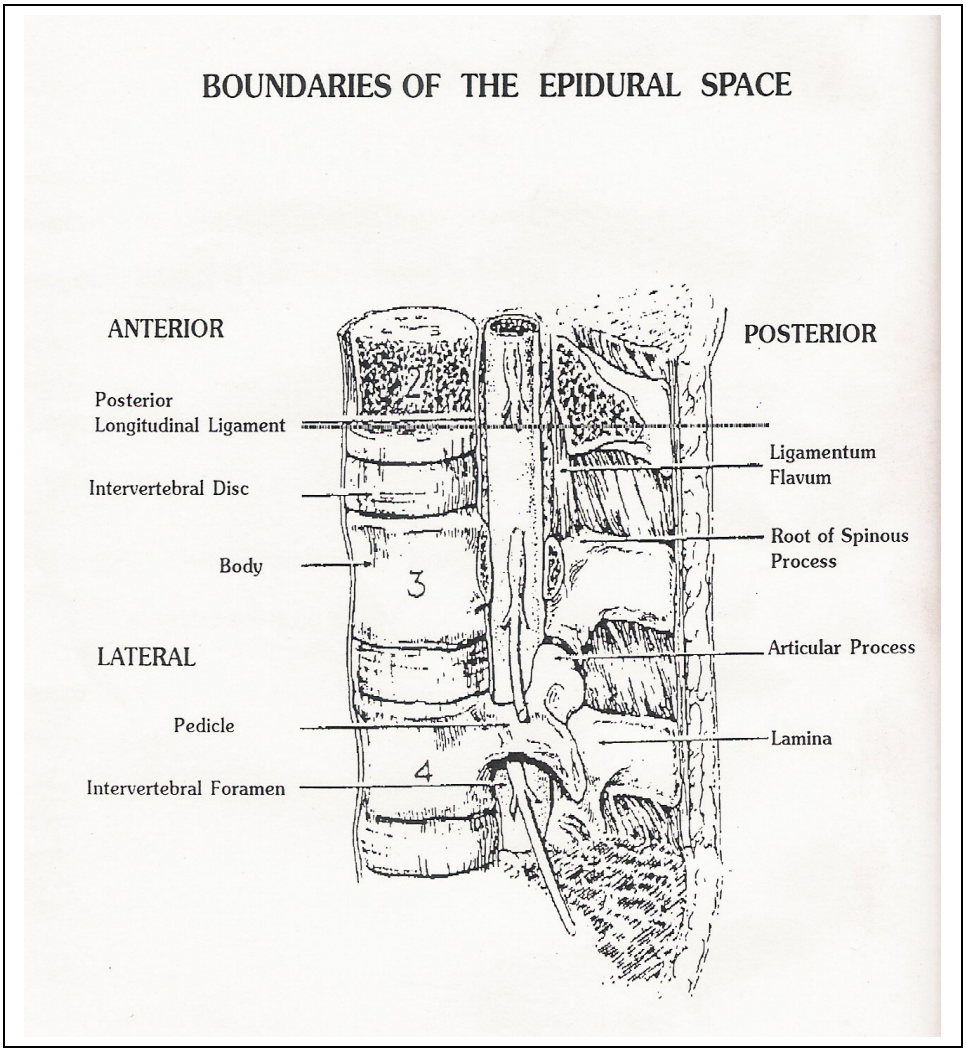
| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Time | | | | | | | | | |
| Score | | | | | | | | | |

Time to get first Analgesia :

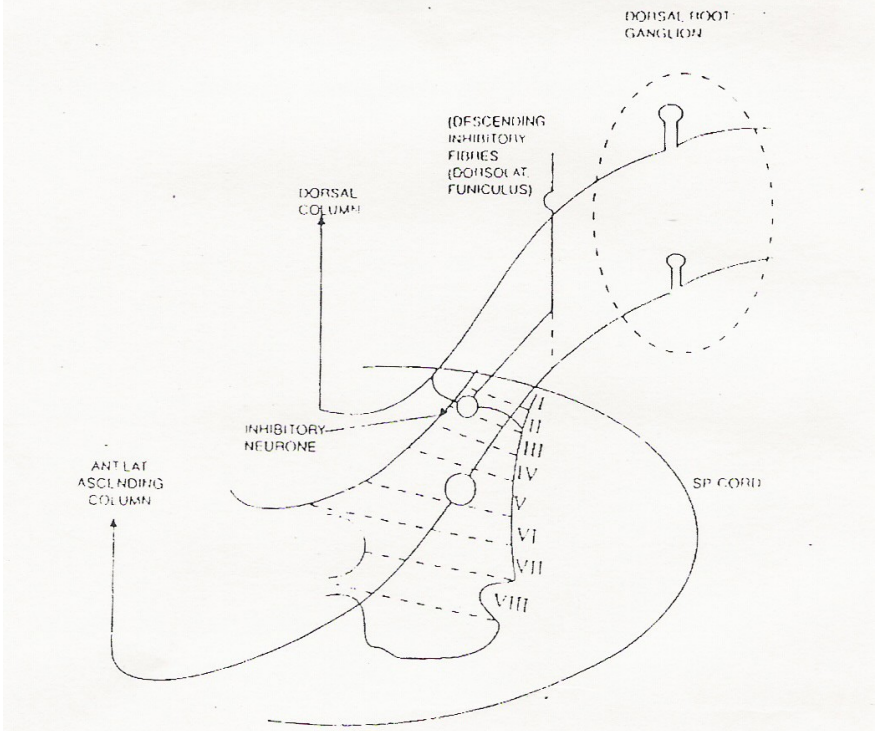
| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | |
| VRS | | | | | | | | | |

Side effects & Complications :

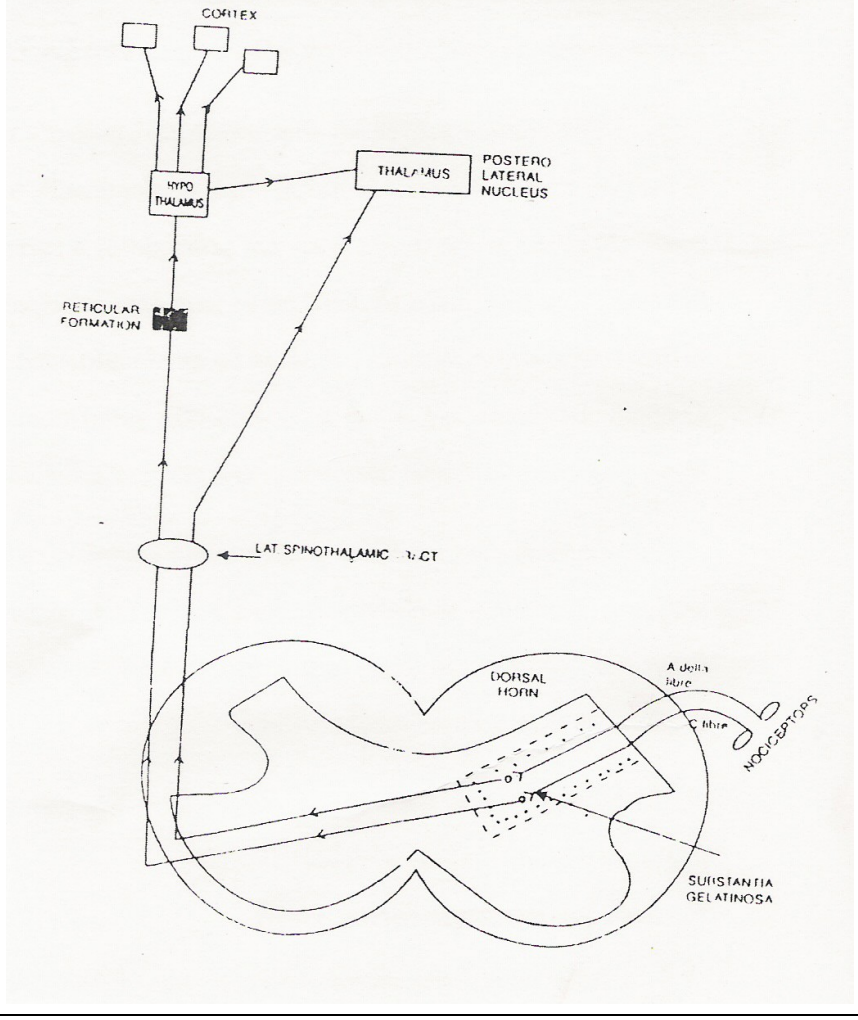
1. Shivering
2. Pruritis
3. Nausea, vomiting
4. Respiratory depression
5. Hypotension
6. Bradycardia


BOUNDARIES OF THE EPIDURAL SPACE
ANTERIOR
POSTERIOR
Posterior
Longitudinal Ligament
Intervertebral Disc
Body
LATERAL
Pedicle
Intervertebral Foramen
Ligamentum
Flavum
Root of Spinous
Process
Articular Process
Lamina
3
4

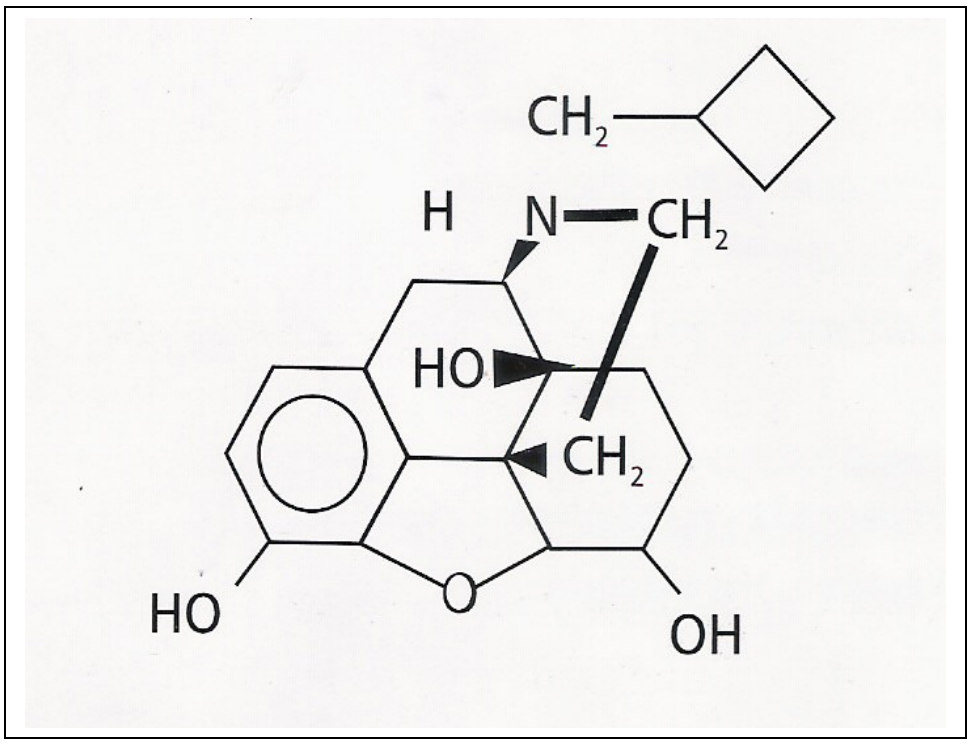
## SPINAL CORD WITH LAMINAE AND THEIR INTERCONNECTIONS



## ORGANISATION OF NEURONAL PATHWAY FOR PAIN



## STRUCTURE OF NULBUPHINE



## STRUCTURE OF BUPIVACAINE